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Detecting Anomalies in Space and Time with Application to Biosurveillance

Fricker, Ronald D.

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Detecting Anomalies in Space and Time with Application to Biosurveillance

Ronald D. Fricker, Jr.

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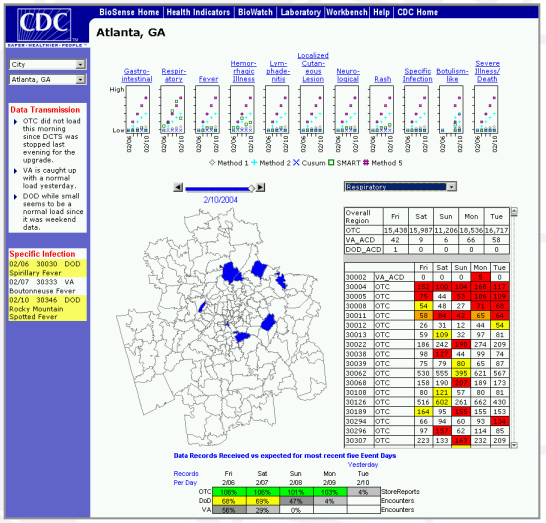
Motivating Problem: Biosurveillance

- "…surveillance using health-related data that precede diagnosis and signal a sufficient probability of a case or an outbreak to warrant further public health response." [1]
- Biosurveillance uses now encompass both "early event detection" and "situational awareness"

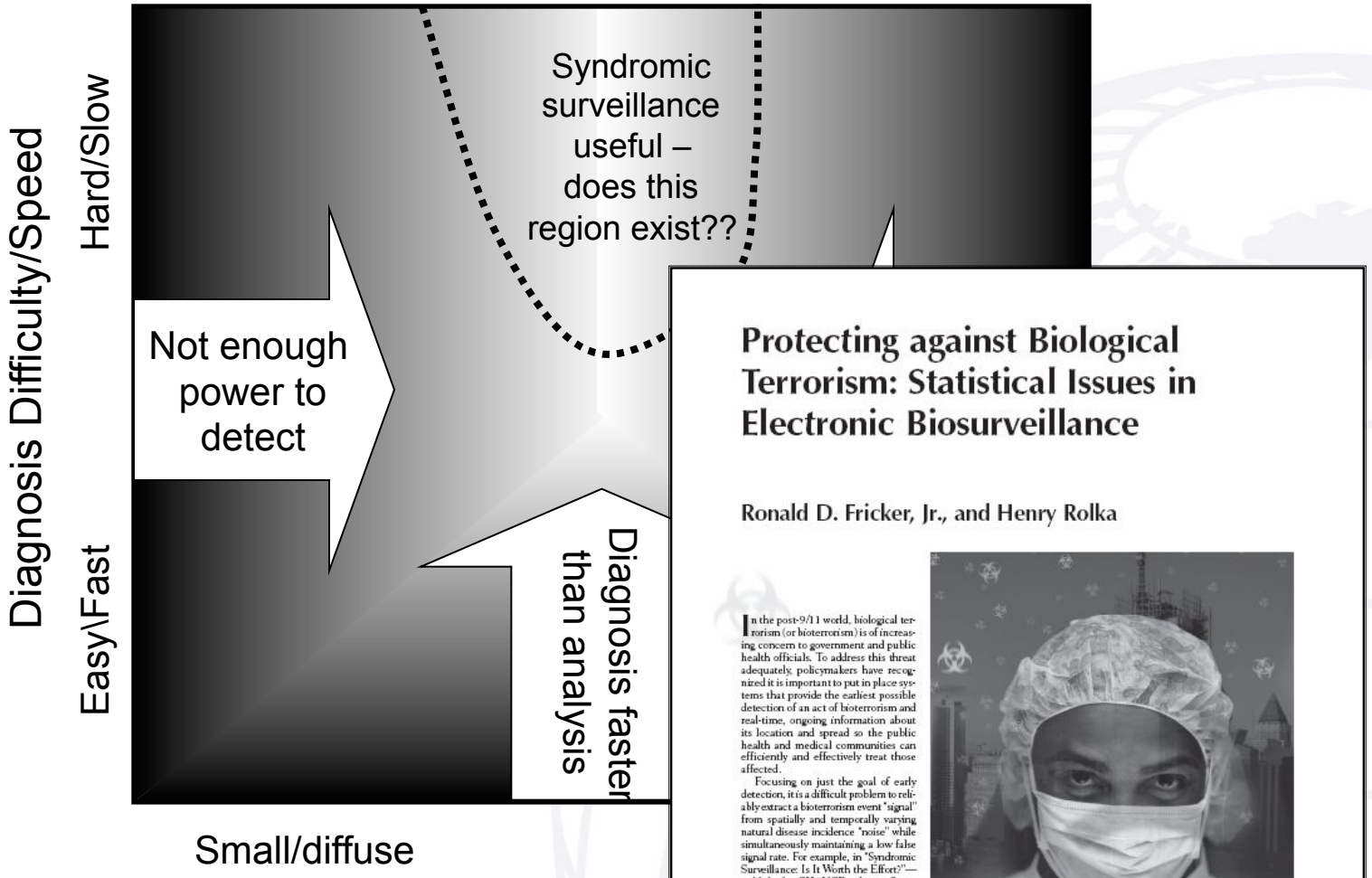


[1] CDC (www.cdc.gov/epo/dphsi/syndromic.htm, accessed 5/29/07)

Definitions

- *Early event detection*: gathering and analyzing data in advance of diagnostic case confirmation to give early warning of a possible outbreak
- *Situational awareness*: the real-time analysis and display of health data to monitor the location, magnitude, and spread of an outbreak

An Aside…



Protecting against Biological Terrorism: Statistical Issues in Electronic Biosurveillance

Ronald D. Fricker, Jr., and Henry Rolka

In the post-9/11 world, biological terrorism (or bioterrorism) is of increasing concern to government and public health officials. To address this threat adequately, policymakers have recognized it is important to put in place systems that provide the earliest possible detection of an act of bioterrorism and real-time, ongoing information about its location and spread so the public health and medical communities can efficiently and effectively treat those affected.

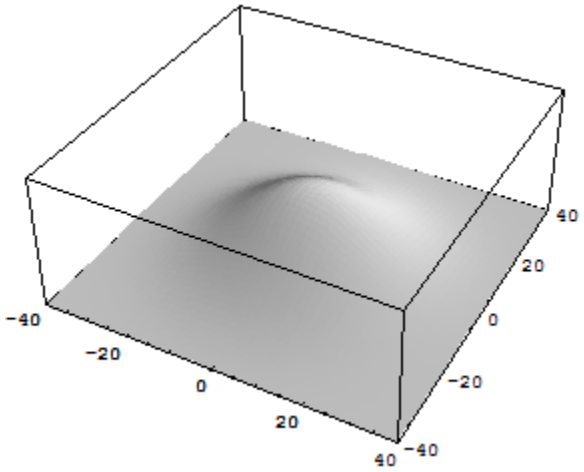
Focusing on just the goal of early detection, it is a difficult problem to reliably extract a bioterrorism event "signal" from spatially and temporally varying natural disease incidence "noise" while simultaneously maintaining a low false signal rate. For example, in "Syndromic Surveillance: Is It Worth the Effort?"—published in *CHANCE*, vol. 17—Stoto, Schonlau, and Mariano evaluated the performance of a number of statistical methods to temporally detect a simulated bioterrorism event and concluded, "Our simulation study gives some indication of the size and speed that outbreaks must attain before they are detectable, and the results are sobering."

4 VOL. 19, NO. 4, 2006

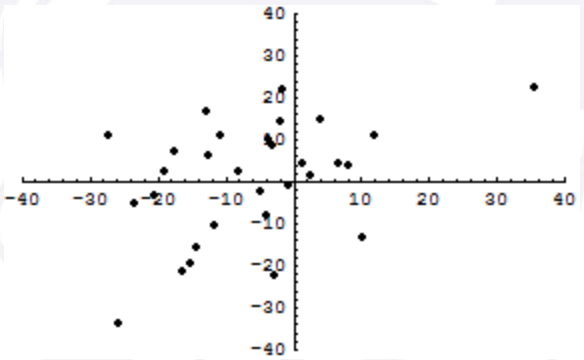
Fricker, R.D., Jr., and H.R. Rolka, Protecting Against Biological Terrori
Statistical Issues in Electronic Biosurveillance, *Chance*, **19**, pp. 4-13, 20

Illustrative Example

- ER patients come from surrounding area
  - On average, 30 per day
    - More likely from closer distances
  - Outbreak occurs at (20,20)
    - Number of patients increase linearly by day after outbreak



(Unobservable) distribution of ER patients' home addresses



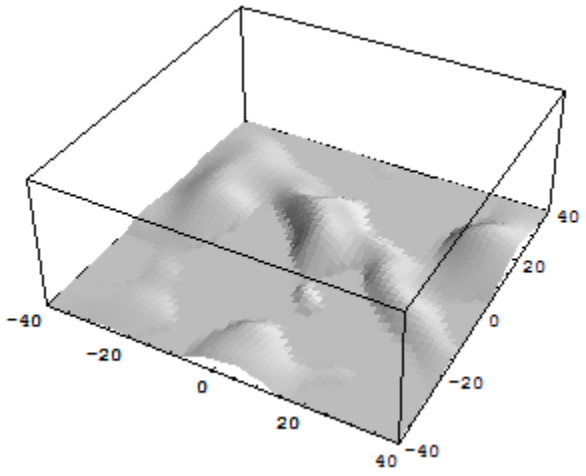
Observed distribution of ER patients' locations

A Couple of Major Assumptions

- Can geographically locate individuals *in a medically meaningful way*
  - Non-trivial problem
  - Data not currently available
- Data is reported in a timely and consistent manner
  - Public health community working this problem, but not solved yet
  - Assuming the above problems away…

Idea: Look at Differences in Kernel Density Estimates

- Construct kernel density estimate (KDE) of "normal" disease incidence using N historical observations
- Compare to KDE of most recent $w+1$ obs



But how to know when to signal?

Solution: Repeated Two-Sample Rank (RTR) Procedure

- Sequential hypothesis test of estimated density heights
- Compare estimated density heights of recent data against heights of set of historical data
  - Single density estimated via KDE on *combined* data
- If no change, heights uniformly distributed
  - Use nonparametric test to assess

Data & Notation

- Let $\mathbf{X}_i = \{X_{1i}, X_{2i}\}$ be a sequence of bivariate observations
  - E.g., latitude and longitude of a case
- Assume a historical sequence $\mathbf{X}_{1-N}, \ldots, \mathbf{X}_0$ is available
  - Distributed iid according to f_0
- Followed by $\mathbf{X}_1, \mathbf{X}_2, \ldots$ which may change from f_0 to f_1 at any time
- Densities f_0 and f_1 unknown

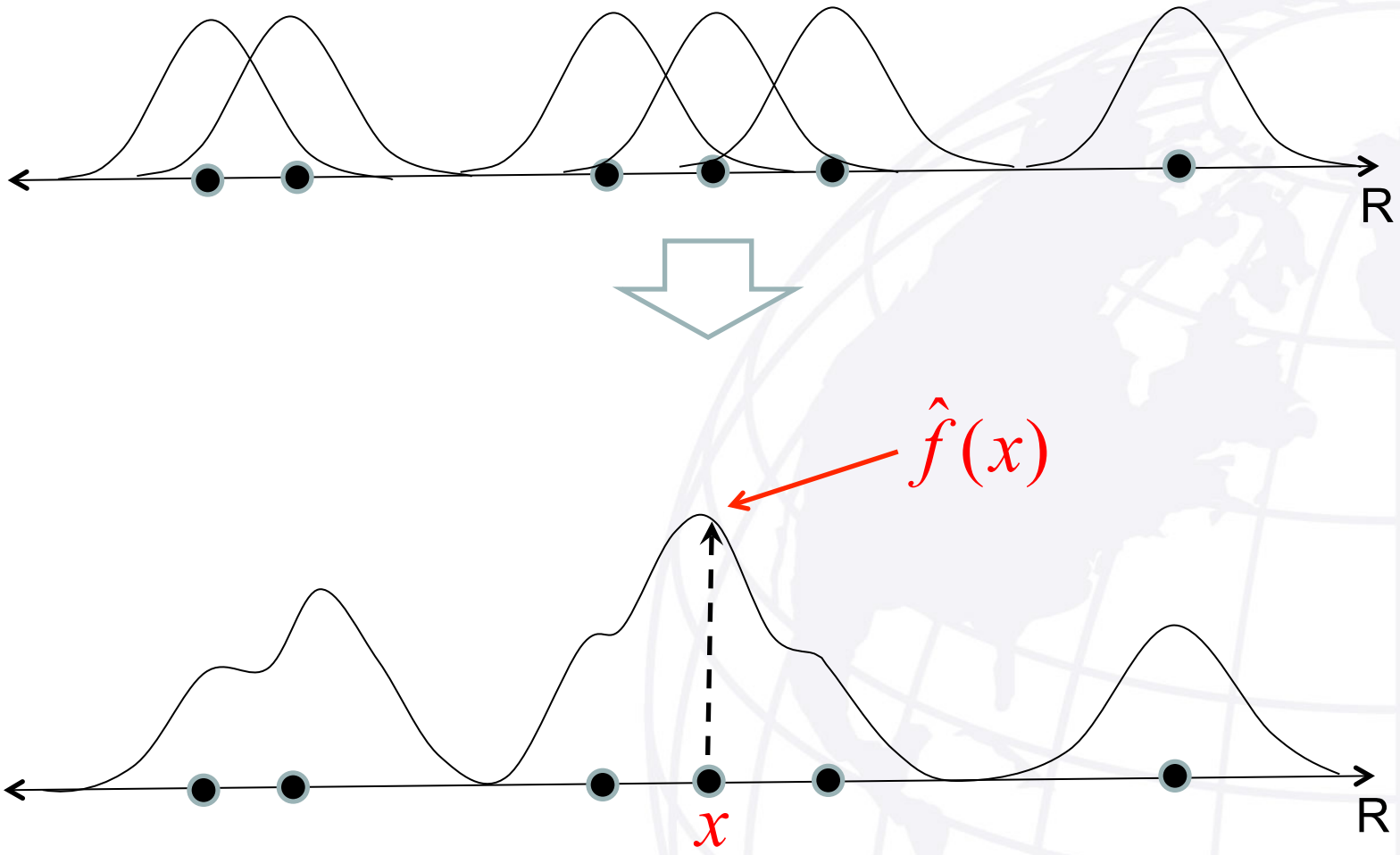
Estimating the Density

- Consider the $w+1$ most recent data points
- At each time period estimate the density

$$\hat{f}_n(\mathbf{x}) = \begin{cases} \dfrac{1}{N+n} \displaystyle\sum_{i=1-N}^{n} k_h(\mathbf{x}, \mathbf{X}_i), & n < w+1 \\ \dfrac{1}{N+w+1} \displaystyle\sum_{i=n-w-N-1}^{n} k_h(\mathbf{x}, \mathbf{X}_i), & n \geq w+1 \end{cases}$$

where k is a kernel function on $\mathbb{R}^2$ with bandwidth set to $h_i = \sigma_i \left(1/\left(N+w+1\right)\right)^{1/6}$

Illustrating Kernel Density Estimation (in one dimension)



Calculating Density Heights

- The density estimate is evaluated at each historical and new point
  - For $n < w+1$

$$\underbrace{\hat{f}_n(\mathbf{X}_{1-N}), \ldots, \hat{f}_n(\mathbf{X}_0)}_{\text{historical observations}}, \underbrace{\hat{f}_n(\mathbf{X}_1), \ldots, \hat{f}_n(\mathbf{X}_n)}_{\text{new observations}}$$

  - For $n \geq w+1$

$$\underbrace{\hat{f}_n(\mathbf{X}_{n-w-N-1}), \ldots, \hat{f}_n(\mathbf{X}_{n-w-1})}_{\text{historical observations}}, \underbrace{\hat{f}_n(\mathbf{X}_{n-w}), \ldots, \hat{f}_n(\mathbf{X}_n)}_{\text{new observations}}$$

Under the Null, Estimated Density Heights are Exchangeable

- *Theorem*: The RTR procedure is asymptotically distribution free
  - I.e., the estimated density heights are exchangeable, so all rankings are equally likely
  - Proof: See Fricker and Chang (2008)
- Means can do a hypothesis test on the ranks each time an observation arrives
  - Signal change in distribution first time test rejects

Comparing Distributions of Heights

- Compute empirical distributions of the two sets of estimated heights:

$$\hat{J}_n(z) = \frac{1}{w+1} \sum_{i=n-w}^{n} I\left\{\hat{f}_n(\mathbf{X}_i) \le z\right\},$$

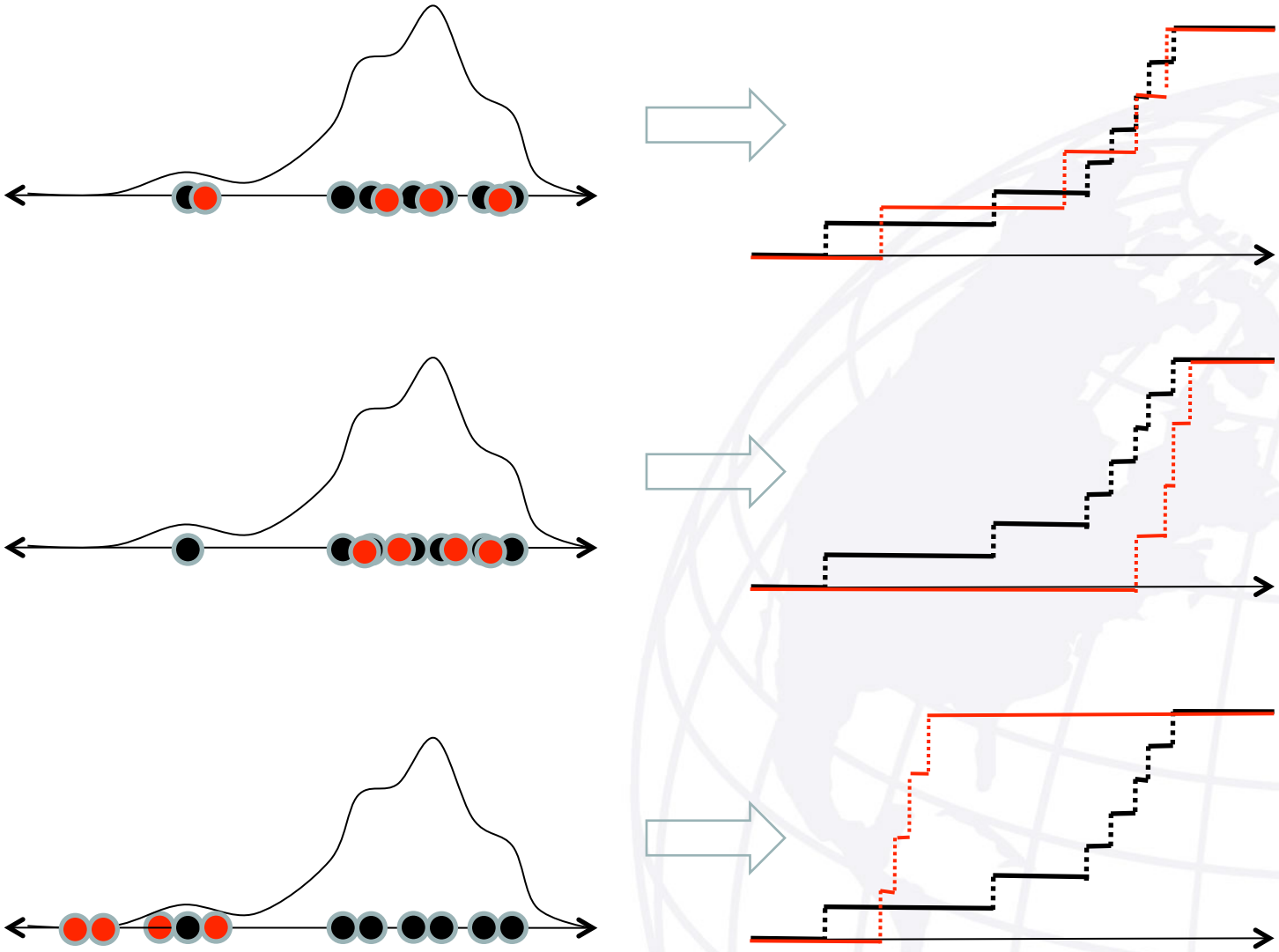
$$\hat{H}_n(z) = \frac{1}{N} \sum_{i=n-w-N-1}^{n-w-1} I\left\{\hat{f}_n(\mathbf{X}_i) \le z\right\}$$

- Use Kolmogorov-Smirnov test to assess:

$$S_n = \max_z \left|\hat{J}_n(z) - \hat{H}_n(z)\right|$$

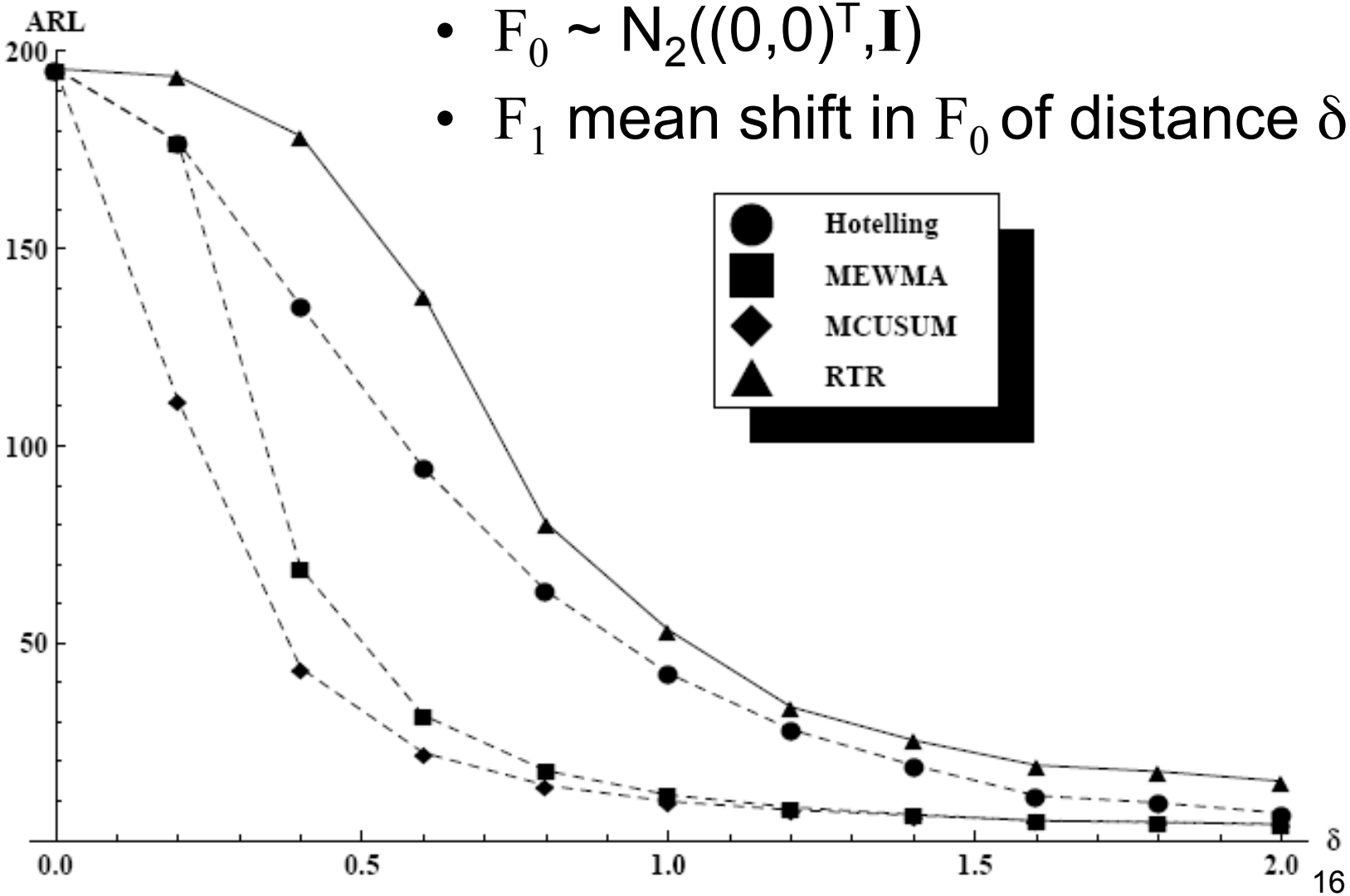
  - Signal at time $t = \min\left\{n : S_n > c\right\}$

Illustrating Changes in Distributions (again, in one dimension)



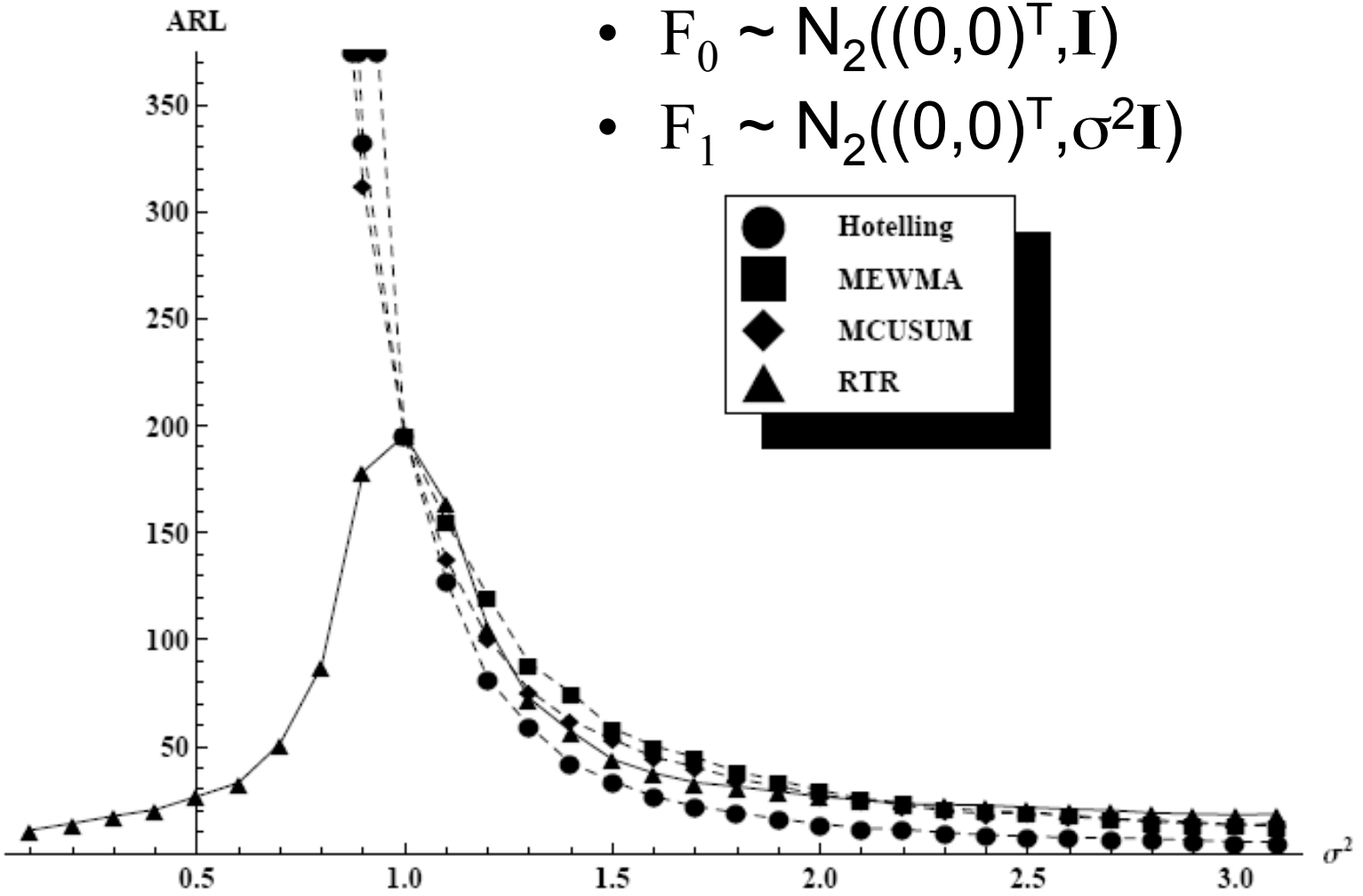
Performance Comparison #1

- $F_0 \sim N_2((0,0)^T, \mathbf{I})$
- F_1 mean shift in F_0 of distance δ



Performance Comparison #2

- $F_0 \sim N_2((0,0)^T, \mathbf{I})$
- $F_1 \sim N_2((0,0)^T, \sigma^2\mathbf{I})$



Comparison Metrics

- How to find c?
  - Use ARL approximation based on Poisson clumping heuristic:

$$A \approx \left[\left(\frac{6.16c\,[c + 0.5/(w+1)]}{1 + (w+1)/N} \right) \exp\left\{ -2\left(c + \frac{1}{2(w+1)} \right)^2 \left(\frac{1}{w+1} + \frac{1}{N} \right)^{-1} \right\} \right]^{-1}$$

- Example: c=0.07754 with N=1,350 and $w+1$=250 gives A=900
  - If 30 observations per day, gives average time between (false) signals of 30 days

Plotting the Outbreak

- At signal, calculate optimal kernel density estimates and plot pointwise differences

$$\Delta_n(\mathbf{x}) = \max\left(\delta, \hat{h}_n(\mathbf{x}) - \hat{g}_n(\mathbf{x})\right)$$

where

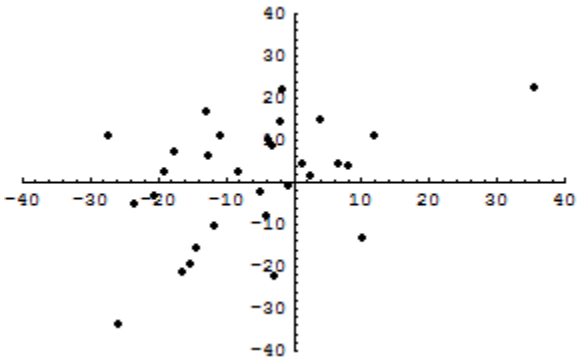
$$\hat{h}_n(\mathbf{x}) = \frac{1}{w+1}\sum_{i=n-w}^{n} k_h\left(\mathbf{x}, \mathbf{X}_i\right)$$

$$\hat{g}_n(\mathbf{x}) = \frac{1}{N}\sum_{i=n-w-N-1}^{n-w-1} k_h\left(\mathbf{x}, \mathbf{X}_i\right)$$

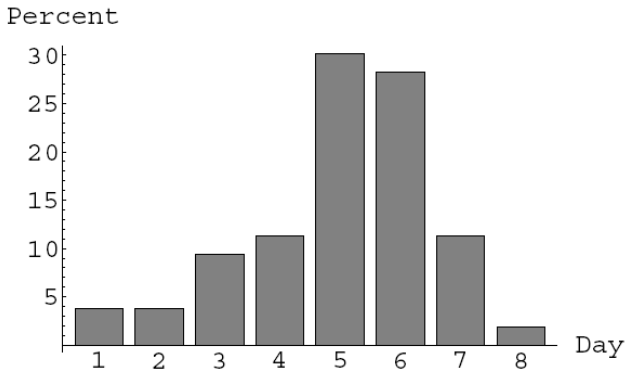
and $h_i = \sigma_i\left(\frac{1}{w+1}\right)^{1/6}$ or $h_i = \sigma_i\left(\frac{1}{N}\right)^{1/6}$

Example Results

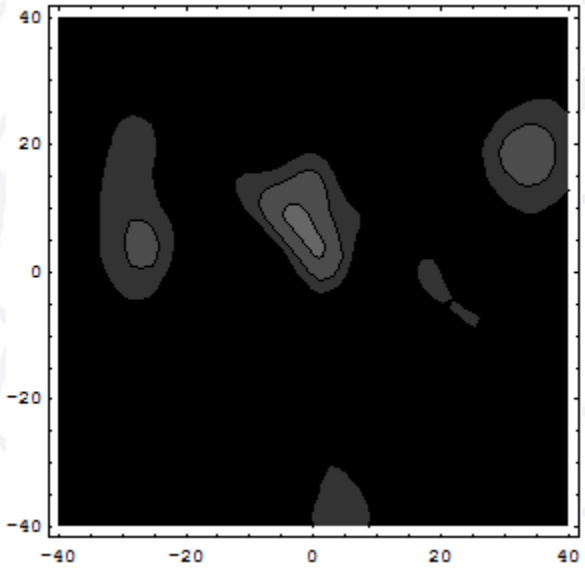
- Assess performance by simulating outbreak multiple times, record when RTR signals
  - Signaled middle of day 5 on average
  - By end of 5th day, 15 outbreak and 150 non-outbreak observations
  - From previous example:



Daily Data

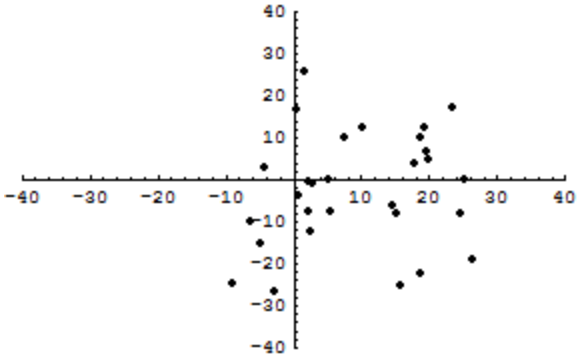


Distribution of Signal Day

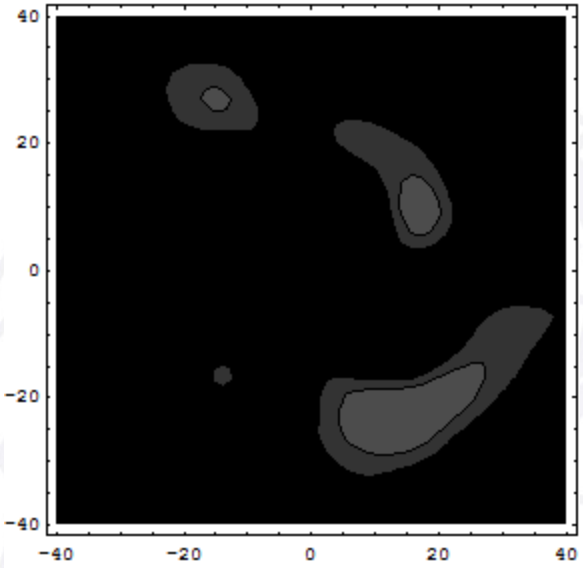


Outbreak Signaled on Day 7 (obs'n # 238)

Same Scenario, Another Sample



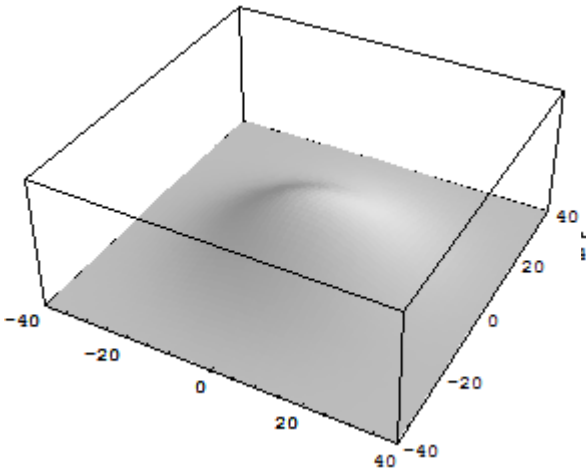
Daily Data



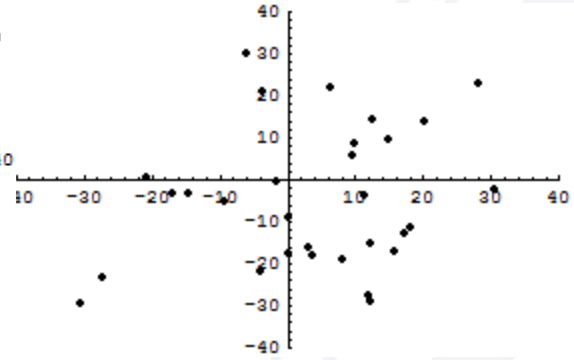
Outbreak Signaled on Day 5 (obs' n # 165)

Another Example

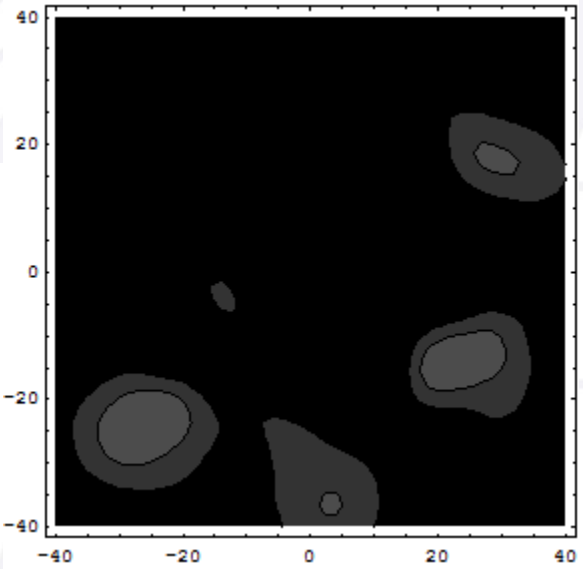
- Normal disease incidence ~ $N(\{0,0\}^t, \sigma^2\mathbf{I})$ with $\sigma=15$
  - Expected count of 30 per day
- Outbreak incidence ~ $N(\{20,20\}^t, 2.2d^2\mathbf{I})$
  - d is the day of outbreak
  - Expected count is $30+d^2$ per day



Unobserved outbreak distribution



Daily data

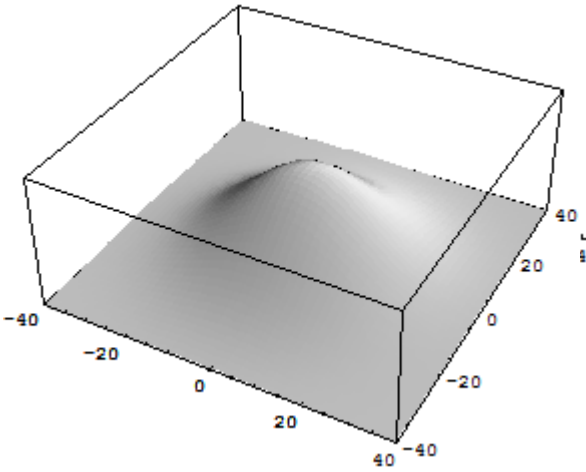


Outbreak signaled on day 1 (obs' n # 2)

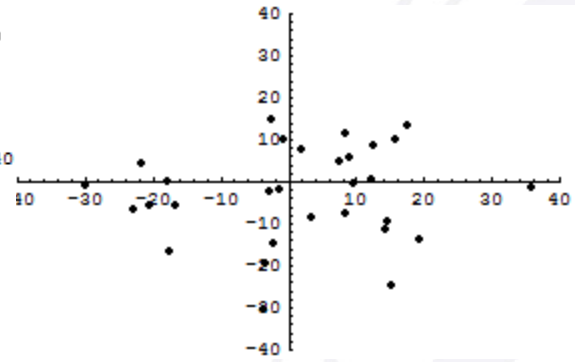
(On average, signaled on day 3-1/2)

And a Third Example

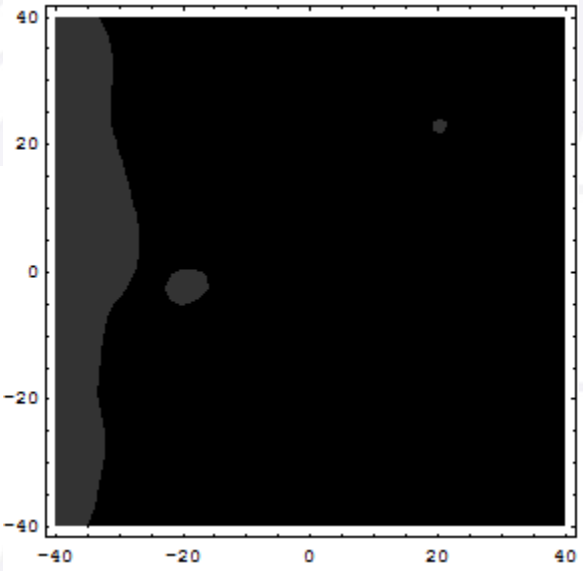
- Normal disease incidence ~ $N(\{0,0\}^t, \sigma^2 \mathbf{I})$ with σ=15
  - Expected count of 30 per day
- Outbreak sweeps across region from left to right
  - Expected count is 30+64 per day



Unobserved outbreak distribution



Daily data



Outbreak signaled on day 1 (obs'n # 11)

(On average, signaled 1/3 of way into day 1)

Advantages and Disadvantages

- Advantages
  - Methodology supports both biosurveillance goals: early event detection *and* situational awareness
  - Incorporates observations sequentially (singly)
    - Most other methods use aggregated data
  - Can be used for more than two dimensions
- Disadvantage?
  - Can't distinguish increase distributed according to f_0
    - Unlikely for bioterrorism attack?
    - Won't detect an general increase in background disease incidence rate
      - E.g., Perhaps caused by an increase in population
      - In this case, advantage not to detect

Selected References

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- Fricker, R.D., Jr., Syndromic Surveillance, in *Encyclopedia of Quantitative Risk Assessment*, Melnick, E., and Everitt, B (eds.), John Wiley & Sons Ltd, pp. 1743-1752, 2008.